2-pyrimioxybenzyl substituted phenyl amine derivatives

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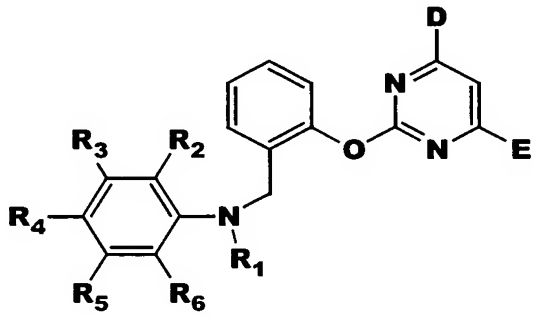
Abstract of **CN1348690**

The present invention discloses 2-pyrimidine oxy benzyl substituted phenylamine derivative herbicide for cotton, rape, wheat fields with the advantages of good effect, low dose, broad spectrum, low poison, no harm to crops etc. Its structural formula is also disclosed as follow: (R2-)(R3-)(R4-)(R5-)(R6-)-benz-N(R1-)-benz-0-1,3-diazine-(D-)-E; where : R1 is not H

CN 1348690A English Translation of Ref 1

Claims

1. A class of pyrimidinyl compound, characterized as 2-pyrimidinyloxy-benzyl-phenylamine derivative, shown by formula (I):



(I)

Wherein,

D and E can be same or different, each being hydrogen, halogen, C_1–C_4 alkyl, C_1–C_4 alkoxy or C_1–C_4 haloalkyl;

R_1 is hydrogen, C_1–C_4 alkanoyl, C_1–C_4 haloalkanoyl, benzoyl or C_1–C_4 alkoxy acetyl;

R_2 is hydrogen, halogen, C_1–C_4 alkyl or trifluoromethyl;

R_3 is hydrogen, halogen, C_1–C_4 alkyl, trifluoromethyl, nitro or cyano;

R_4 is hydrogen, halogen, C_1–C_4 alkyl, C_1–C_4 alkoxy, C_1–C_4 alkoxycarbonyl, trifluoromethyl, cyano, carboxy or its alkali metal, alkali earth metal, transition metal or ammonium salt;

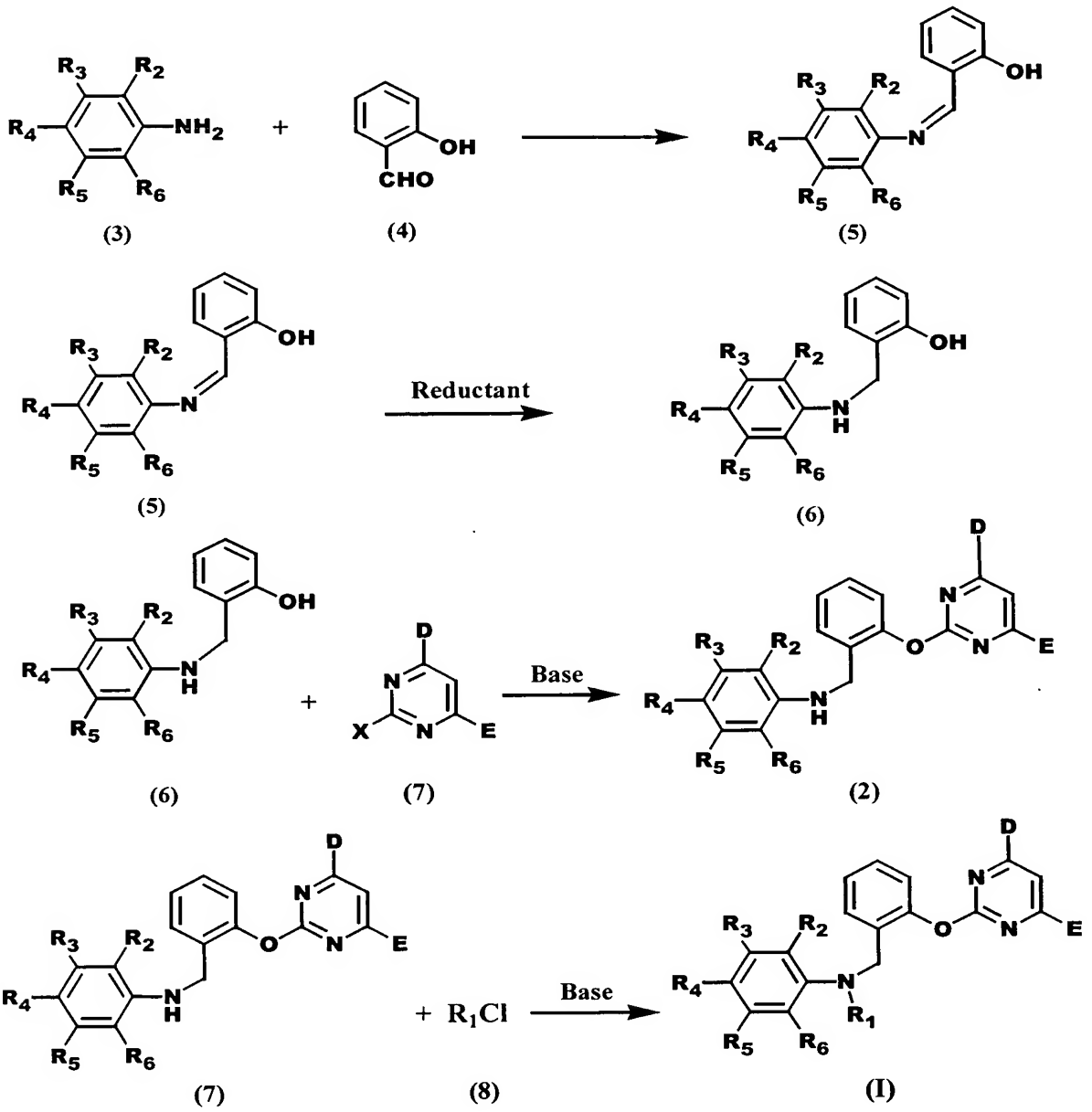
R_5 is hydrogen or halogen;

R_6 is hydrogen, halogen or C_1–C_4 alkyl.

2. The 2-pyrimidinyloxy-benzyl-phenylamine derivative of Claim 1 with structure described in formula (I), characterized in that both D and E are methoxy, or one of which being methoxy, another being chloro or methyl; R_1 is hydrogen, acetyl, chloroacetyl, dichloroacetyl, benzoyl or methoxyacetyl; R_2 is hydrogen, fluoro, chloro, bromo, iodo, methyl, ethyl or trifluoromethyl; R_3 is hydrogen, chloro, fluoro, methyl, trifluoromethyl, nitro or cyano; R_4 is hydrogen, fluoro, chloro, bromo, iodo, methyl, trifluoromethyl, methoxy, C_1–C_4 alkoxycarbonyl, carboxy or its sodium or potassium salt; R_5 is hydrogen or chloro; R_6 is hydrogen, methyl or ethoxy;

3. The 2-pyrimidinyloxy-benzyl-phenylamine derivative of Claims 1 or 2, characterized in that both D and E in formula (I) are methoxy; R_1 is hydrogen;

4. A process for preparing the 2-pyrimidinyloxy-benzyl-phenylamine derivative of Claims 1, 2 or 3, characterized in the reaction formula described below:



(Where, each substituent represents group that described in Claims 1, 2 or 3, R ≠ H, X = halogen or methylsulfonyl)

Firstly substituted aniline (3) and salicylal (4) with a molar ratio of 1: (1.0~1.2), are dissolved in an alcohol solvent. The reaction takes 20 ~ 60 minutes at a temperature range from room temperature to the boiling point of the solvent, to afford intermediate (5). Then to the alcohol solution is added either sodium borohydride or potassium borohydride. The reduction gives intermediate (6). After the solvent is removed, the reaction with 2-halo-4,6-substituted pyrimidine or 2-methylsulfonyl-4,6-substituted pyrimidine (7) (the said 4,6-substituted group is the substitutent D and E as described in Claim 1) with a molar ratio of 1 : (1.0~1.1) in an ether solvent and a basic condition, gives compound (2) as shown in formula (I) (R_1 = H). Further reaction of this compound (2) with acid chloride (8) in a basic condition, gives compound as shown in formula (I) ($R_1 \neq$ H).

5. The 2-pyrimidinyloxy-benzyl-phenylamine derivative of Claim 1, 2 or 3, characterized to have high herbicidal activity. It may be used as an active ingredient to formulate pre- or pro-emergency herbicide, to apply in farm field such as cotton, rape and wheat to control grass, broadleaf weeds and sedges.

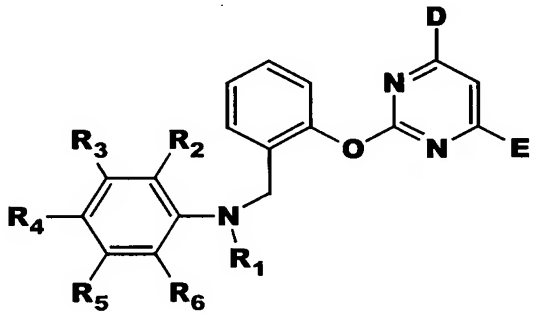
2-Pyrimidinyloxy-Benzyl-Phenylamine Derivatives

The present invention relates to pyrimidinyl compound, especially 2-pyrimidinyloxy-benzyl-phenylamine derivatives, their preparation processes as well as the application and formulation as herbicides.

Nowdays the agricultural modernization demands high effective, low dosage, crop- and environmental-friendly new herbicide provided, in order to reduce the labour force, to promote agricultural mechanization and modernization, and to increase the crop productivity.

The effectiveness of various 2-phenoxy-pyrimidine derivatives as herbicide is known. For instance, patent US4,906,285 demonstrates that the bi-pyrimidine salicylic acid derivatives have broad spectrum of herbicidal activity. Patent US4,932,999 on the other side, discloses the excellent herbicidal activity of the pyrimidinyl thiosalicylic acid derivatives over the perennial and annual weeds. However these herbicides are only suitable to use in the cotton and rice field. They can, in various degrees, damage the rape.

Base on the demand of social development and also to extend application range in order to find the suitable herbicide for rape field, the present inventor extends the lead compound on the basis of the existing inventions to develop a class of 2-pyrimidinyloxy-benzyl-phenylamine derivatives, shown as formula (I).



(I)

wherein formula (I),

D and E can be same or different, each being hydrogen, halogen, C_1–C_4 alkyl, C_1–C_4 alkoxy or C_1–C_4 haloalkyl, preferable both D and E being methoxy, or one of them being methoxy, another being chloro or methoxy, most particularly both of D and E being methoxy;

R_1 is hydrogen, C_1–C_4 alkanoyl, C_1–C_4 haloalkanoyl, benzoyl or C_1–C_4 alkoxy acetyl, preferable being hydrogen, acetyl, chloroacetyl, dichloroacetyl, benzoyl or methoxyacetyl, especially being hydrogen, chloroacetyl or methoxyacetyl, most particularly being hydrogen;

R_2 is hydrogen, halogen, C_1–C_4 alkyl or trifluoromethyl, particularly being hydrogen, fluoro, chloro, bromo, iodo, methyl, ethyl or trifluoromethyl;

R_3 is hydrogen, halogen, C_1–C_4 alkyl, trifluoromethyl, nitro or cyano, particularly being hydrogen, fluoro, chloro, methyl, trifluoromethyl, nitro or cyano;

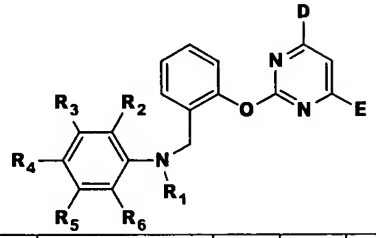
R_4 is hydrogen, halogen, C_1–C_4 alkyl, C_1–C_4 alkoxy, C_1–C_4 alkoxycarbonyl, trifluoromethyl, cyano, carboxy or its alkali metal, alkali earth metal, transition metal or ammonium salt, particularly being hydrogen, fluoro, chloro, bromo, iodo, methyl, trifluoromethyl, methoxy, C_1–C_4 alkoxycarbonyl, carboxy or its sodium, potassium or ammonium salt;

R_5 is hydrogen or halogen, particularly hydrogen, chloro;

R_6 is hydrogen, halogen or C_1–C_4 alkyl, particularly hydrogen, methyl or ethyl.

The present inventor has synthesized a series of compound by using molecular design, *i.e.*, to change D and E and also, various substituents from R_1 to R_6 as well as their various combinations. The herbicidal activities have been evaluated by the biologists. Some compounds with high activity were selected. These compound are concluded in Table 1.

Table 1



Compound No.	D	E	R_1	R_2	R_3	R_4	R_5	R_6	Elemental analysis(%)			Mass spectrum M^+
									C	H	N	
1	OCH_3	OCH_3	H	H	H	Br	H	H	54.68	4.30	10.20	415
2	OCH_3	OCH_3	H	H	H	I	H	H	49.11	3.86	9.00	463
3	OCH_3	OCH_3	H	H	H	$CO_2(CH_2)_2CH_3$	H	H	65.10	5.88	9.99	423
4	OCH_3	OCH_3	H	H	H	OCH_3	H	H	65.33	5.75	11.25	367
5	OCH_3	OCH_3	$COCH_2Cl$	H	H	$CO_2(CH_2)_2CH_3$	H	H	60.21	5.28	8.30	499
6	OCH_3	OCH_3	$COCH_2Cl$	H	H	OCH_3	H	H	59.25	4.99	9.40	443
7	OCH_3	OCH_3	$COCH_2CH_3$	H	H	I	H	H	50.70	4.28	8.21	519
8	OCH_3	OCH_3	$COCH_3$	H	H	I	H	H	49.88	4.00	8.11	505
9	OCH_3	OCH_3	$CO(CH_2)_3Cl$	H	H	Br	H	H	53.11	4.50	8.10	519
10	OCH_3	OCH_3	COPh	H	H	Br	H	H	60.01	4.28	8.09	519
11	OCH_3	OCH_3	$COCHCl_2$	H	H	Br	H	H	47.77	3.47	7.91	527
12	OCH_3	OCH_3	$COCH_2CH_3$	H	H	Br	H	H	55.81	4.65	8.72	471
13	OCH_3	OCH_3	$COCH_2Cl$	H	H	Br	H	H	51.22	3.89	8.44	491

Continuation of Table 1

Compound No.	D	E	R_1	R_2	R_3	R_4	R_5	R_6	Elemental analysis(%)			Mass spectrum M^+
									C	H	N	
14	OCH_3	OCH_3	$COCHCl_2$	H	H	OCH_3	H	H	55.00	4.40	8.66	477
15	OCH_3	OCH_3	$CO(CH_2)_3Cl$	H	H	OCH_3	H	H	61.12	5.60	8.78	471
16	OCH_3	OCH_3	H	Cl	H	H	Cl	H	56.30	4.22	10.33	405
17	OCH_3	OCH_3	H	CH_3	H	H	Cl	H	62.07	5.25	10.88	385
18	OCH_3	OCH_3	$COCH_2Cl$	Cl	H	H	Cl	H	52.11	3.71	8.56	481
19	OCH_3	OCH_3	$COCH_2Cl$	CH_3	H	Cl	H	H	57.25	4.59	9.20	461
20	OCH_3	OCH_3	H	F	H	H	H	H	64.09	5.10	11.88	355
21	OCH_3	OCH_3	H	Cl	H	H	H	H	61.21	4.86	11.54	371
22	OCH_3	OCH_3	H	H	H	Cl	H	H	61.29	4.89	11.33	371
23	OCH_3	OCH_3	H	Cl	Cl	H	H	H	56.30	4.21	10.50	405
24	OCH_3	OCH_3	H	H	H	CH_3	H	H	68.25	5.99	11.88	351
25	OCH_3	OCH_3	H	H	Cl	Cl	H	H	56.06	4.14	10.44	405
26	OCH_3	OCH_3	H	H	Cl	H	H	H	61.50	4.86	11.50	371
27	OCH_3	OCH_3	$COCH_2Cl$	F	H	H	H	H	58.28	4.35	9.66	431
28	OCH_3	OCH_3	$COCH_2Cl$	Cl	H	H	H	H	56.21	4.30	9.50	447
29	OCH_3	OCH_3	$COCH_2Cl$	H	H	Cl	H	H	56.20	4.21	9.52	447
30	OCH_3	OCH_3	$COCH_2Cl$	Cl	Cl	H	H	H	52.17	3.75	8.56	481
31	OCH_3	OCH_3	$COCH_2Cl$	H	H	CH_3	H	H	61.68	5.20	9.87	427

Continuation of Table 1

Compound No.	D	E	R_1	R_2	R_3	R_4	R_5	R_6	Elemental analysis(%)			Mass spectrum M^+
									C	H	N	
32	OCH_3	OCH_3	$COCH_2Cl$	H	Cl	Cl	H	H	52.15	3.80	8.55	481
33	OCH_3	OCH_3	$COCH_2Cl$	H	Cl	H	H	H	56.18	4.30	9.39	447
34	OCH_3	OCH_3	H	CH_3	Cl	H	H	H	62.22	5.25	10.79	385
35	OCH_3	OCH_3	H	CH_3	H	H	H	H	68.25	5.89	11.88	351
36	OCH_3	OCH_3	H	H	Cl	H	Cl	H	56.22	4.14	10.45	405
37	OCH_3	OCH_3	H	Cl	H	Cl	H	H	56.09	4.17	10.33	405
38	OCH_3	OCH_3	H	CH_3	H	CH_3	H	H	69.01	6.35	11.64	365
39	OCH_3	OCH_3	$COCH_2Cl$	CH_3	H	H	H	H	61.76	5.21	9.78	427
40	OCH_3	OCH_3	$COCH_2Cl$	H	Cl	H	Cl	H	52.33	3.69	8.79	481
41	OCH_3	OCH_3	$COCH_2Cl$	Cl	H	Cl	H	H	52.40	3.77	8.55	481
42	OCH_3	OCH_3	$COCH_2Cl$	CH_3	H	CH_3	H	H	62.45	5.49	9.70	441
43	OCH_3	OCH_3	$COCH_2Cl$	CH_3	H	H	H	CH_3	62.60	5.41	9.66	441
44	OCH_3	OCH_3	H	CF_3	H	H	H	H	59.33	4.48	10.45	405
45	OCH_3	OCH_3	$COCH_2Cl$	CF_3	H	H	H	H	54.90	4.01	8.88	481
46	OCH_3	OCH_3	H	H	H	CF_3	H	H	59.27	4.40	10.30	405
47	OCH_3	OCH_3	$COCH_2Cl$	H	H	CF_3	H	H	54.79	3.99	8.56	481
48	OCH_3	OCH_3	$COCH_2Cl$	H	H	I	H	H	46.80	3.54	7.88	539
49	OCH_3	OCH_3	H	H	F	H	H	H	64.33	5.11	11.77	355

Continuation of Table 1

Compound No.	D	E	R_1	R_2	R_3	R_4	R_5	R_6	Elemental analysis(%)			Mass spectrum M^+
									C	H	N	
50	OCH_3	OCH_3	$COCH_2Cl$	H	F	H	H	H	58.29	4.35	9.90	431
51	OCH_3	OCH_3	H	H	I	H	H	H	49.25	3.85	9.11	463
52	OCH_3	OCH_3	$COCH_2Cl$	H	I	H	H	H	46.66	3.59	7.79	539
53	OCH_3	OCH_3	H	H	CH_3	CH_3	H	H	69.20	6.35	11.56	365
54	OCH_3	OCH_3	$COCH_2OCH_3$	H	H	Cl	H	H	59.36	4.90	9.40	443
55	OCH_3	OCH_3	H	H	CF_3	H	H	Cl	54.53	3.81	9.66	439
56	OCH_3	OCH_3	H	C_2H_5	H	H	H	C_2H_5	70.15	6.82	10.78	393
57	OCH_3	OCH_3	H	I	H	H	H	H	49.19	3.80	9.14	463
58	OCH_3	OCH_3	$COCH_2OCH_3$	H	F	H	H	H	61.68	5.10	9.69	427
59	OCH_3	OCH_3	$COCH_2OCH_3$	H	H	I	H	H	49.20	4.14	7.72	535
60	OCH_3	OCH_3	$COCH_2OCH_3$	H	Cl	Cl	H	H	55.26	4.35	8.88	477
61	OCH_3	OCH_3	$COCH_2Cl$	H	CH_3	CH_3	H	C_2H_5	62.55	5.40	9.60	441
62	OCH_3	OCH_3	$COCH_2Cl$	C_2H_5	H	H	H	Cl	63.89	5.97	8.99	469
63	OCH_3	OCH_3	$COCH_2Cl$	H	CF_3	H	H	H	51.30	3.43	8.15	515
64	OCH_3	OCH_3	$COCH_2Cl$	I	H	H	H	H	46.88	3.53	7.78	539
65	OCH_3	OCH_3	$COCH_2OCH_3$	H	Cl	H	H	H	59.45	4.91	9.50	443
66	OCH_3	OCH_3	$COCH_2OCH_3$	H	I	H	H	H	49.50	4.17	7.85	535
67	OCH_3	OCH_3	H	H	H	H	H	H	67.70	5.63	12.55	337

Continuation of Table I

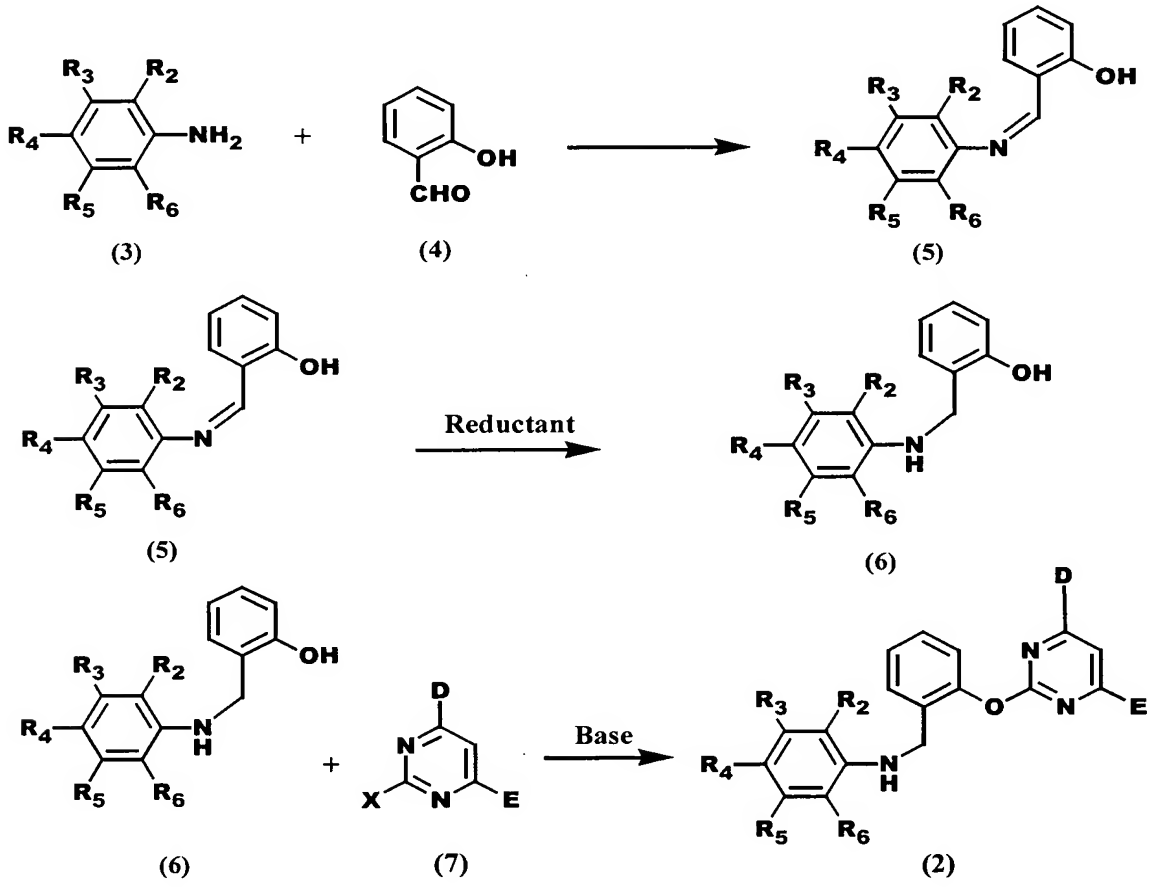
Compound No.	D	E	R_1	R_2	R_3	R_4	R_5	R_6	Elemental analysis(%)			Mass spectrum M^+
									C	H	N	
68	OCH_3	OCH_3	H	CH_3	H	Br	H	H	55.68	4.70	9.92	429
69	OCH_3	OCH_3	H	Br	H	H	H	H	54.77	4.41	10.20	415
70	OCH_3	OCH_3	H	H	H	F	H	H	64.40	5.10	11.89	355
71	OCH_3	OCH_3	H	H	CF_3	H	H	H	59.29	4.50	10.34	405
72	OCH_3	OCH_3	H	H	Cl	F	H	H	58.44	4.31	10.77	389
73	OCH_3	OCH_3	H	CH_3	NO_2	H	H	H	60.49	5.10	14.30	395
74	OCH_3	OCH_3	H	H	NO_2	CH_3	H	H	60.56	5.08	14.20	395
75	OCH_3	OCH_3	$COCH_2Cl$	H	H	H	H	H	60.88	4.80	10.16	413
76	OCH_3	OCH_3	H	H	H	CN	H	H	66.21	4.94	15.44	362
77	OCH_3	OCH_3	H	H	CN	H	H	H	66.29	4.99	15.56	362
78	OCH_3	OCH_3	H	H	H	CO_2CH_3	H	H	63.77	5.25	10.70	395
79	OCH_3	OCH_3	H	H	H	$CO_2C_2H_5$	H	H	64.45	5.60	10.41	409
80	OCH_3	OCH_3	H	H	H	$CO_2C_4H_9$-n	H	H	65.88	6.21	9.56	437
81	OCH_3	OCH_3	H	H	H	$CO_2CH(CH_3)_2$	H	H	65.33	5.88	9.78	423
82	OCH_3	OCH_3	H	H	H	CO_2Na	H	H	59.65	4.52	10.45	403
83	OCH_3	OCH_3	H	H	H	CO_2K	H	H	57.41	4.26	10.11	419
84	OCH_3	OCH_3	H	H	H	CO_2H	H	H	62.79	4.89	11.20	381
85	Cl	OCH_3	H	H	H	$CO_2C_2H_5$	H	H	60.88	4.80	10.31	413

Compound No.	D	E	R_1	R_2	R_3	R_4	R_5	R_6	Elemental analysis(%)			Mass spectrum M^+
									C	H	N	
86	CH_3	OCH_3	H	H	H	$CO_2C_2H_5$	H	H	67.30	5.81	10.59	393
87	OCH_3	OCH_3	H	H	H	$CO_2H \cdot NH(CH_3)_2$	H	H	61.99	6.19	13.25	381

The bio-test shows that, the 2-pyrimidinyloxy-benzyl-phenylamine derivatives as shown in formula (I) is effective against major grass and broadleaved weeds. The molecules have favourable toxicological, ecotoxicological and environmental profiles with low risk potentials to plants. Therefore, they are active ingredients to formulate herbicide.

There is big variety of compounds from the present invention. However, the formulas are similar so that they are homologous compound. Therefore, they can be prepared in a similar manner. The synthetic method that the present inventor uses is described below:

1. The synthetic method for compound as shown in formula (I) (R_1 = H), has three steps. It may be represented by the reaction equation below:



The substituted groups that R_2, R_3, R_4, R_5, R_6, and D, E represent in each compound of above equations are the same as previous described. X is halogen or methylsulfonyl group.

That is to say, that the synthesis of compound (2) shown by formula (I) (R_1 = H) of the present invention, is proceeded by firstly dissolving substituted aniline (3) and salicylal (4) in a molar of 1 : (1.0~1.2) in alcohol solvent such as methanol, ethanol or propanol, at a temperature range from room temperature to the boiling point of the solvent for 20 ~ 60 minutes, to afford intermediate (5). The reaction may be taken place without the presence of the catalyst. However the addition of a catalyst and the removal of water by azeotropic distillation can promote the speed as well as the yield of the reaction. The catalyst used in the reaction maybe *p*-toluenesulfonic acid, methanesulfonic acid, sulfuric acid or hydrochloride acid.

Besides the alcohol solvent used in the reaction, arene such as benzene, toluene or xylene; halo-alkane such as dichloromethane, dichloroethane or chloroform; ether solvent such as tetrahydrofuran or dioxane; ketone solvent such as acetone or methyl *i*-butyl ketone; or *N,N*-dimethylformamide or dimethylsulfoxide; or acetonitrile; and the mixture thereof, can be used as the solvent.

Then, intermediate (5) obtained from step one, dissolved in an alcohol solvent such as methanol, ethanol or propanol, is reduced at room temperature to give intermediate (6) with the presence of a reductant such as sodium borohydride or potassium borohydride.

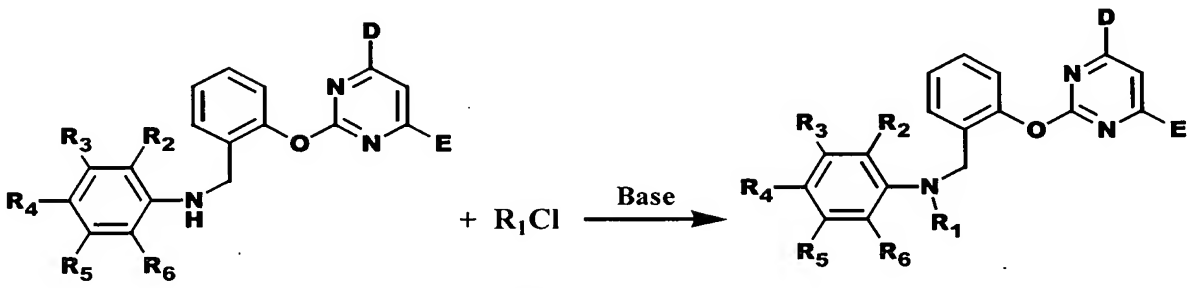
Thirdly, the reaction of intermediate (6) and 2-halo-4,6-substituted pyrimidine or 2-methylsulfonyl-4,6-substituted pyrimidine (7) with a molar ratio of 1 : (1.0~1.2) in a solvent with the present of a base, gives product of the present invention, shown as compound (2) in formula (I) (R_1 = H). In the reaction step, the base used can be alkali metal such as sodium or potassium, or alkali hydride such as sodium hydride or potassium hydride, or alkali earth hydride such as calcium hydride, or metal alkoxide such as sodium alkoxide or potassium alkoxide, or alkali carbonate such as sodium carbonate or potassium carbonate, or organic amine such as triethylamine or pyridine.

The solvent used in step three can be an arene solvent such as benzene, toluene or xylene, an alcohol solvent such as methanol, ethanol or propanol, an ether solvent such as tetrahydrofuran or dioxane, a ketone solvent such as acetone or methyl *i*-butyl ketone, *N,N*-dimethylformamide, dimethylsulfoxide, or acetonitrile; and the mixture thereof.

The synthetic method for compound as shown in formula (I) ($R_1 \neq H$):

As described previously, the compound obtained from the three-step reaction, shown as formula (I) (R_1 = H) compound (2), is one of the active ingredient for herbicide we need. If it is further treated

with acid chloride (8) in a solvent in the presence of a base, a compound too with herbicidal activity shown in formula (I) ($R_1 \neq H$) can be obtained. The reaction may be represented by equation below:



(7) (8) (I)

D and E, R_1-R_6 in the reaction equation are the same as described previously ($R_1 \neq H$).

The said reaction temperature range is room temperature to the boiling point of the solvent. The solvent and base used in the reaction are the same as those in the third step during the synthesis of compound (2) shown previously in formula (I) ($R_1 = H$).

The 2-pyrimidinyloxy-benzyl-phenylamine derivatives of the present invention can be synthesized simply. The products have excellent herbicidal activities. They are effective active ingredients for formulating herbicides.

The compounds of formula (I) provided by the present invention and the preparations can effectively control most of weeds in the field. They can effectively control some annual grass in low dosage of 45~75 g ai/ha (g ai/ha refers to one gram active ingredient per hectare, same hereinafter); effectively control broadleaf weeds and sedges in high dosage of 150~300 g ai/ha, for instance, *Echinochloa crusgalli, Digitaria sanguinalis, Eleusine indica, Setaria viridis, Poa annua, Avena fatua, Alopecurus aequalis, Alopecurus japonicus, Amaranthus retroflexus, Amaranthus spinosus, Chenopodium album, Brassica juncea, Portulaca oleracea, Acalypha australis, Cyperus diffformis, Leptochloa chinensis, Cyperus rotundus, Fimbristylis miliacea, Veronica didyma, Stallaria media, Vicia sativa, Stellaria alsine, Erigeron annuus, Sagittaria sagittifolia, Convolvulus arvensis,* and so on. As herbicides, they have following advantages and characteristics:

1. Excellent activity of weed control, effective even at a low dosage;
2. Having high effective post-emergency weed control at a low dosage, pre-emergency weed control also at a relatively high dosage;

3. Having a broad spectrum of weed control, that can control major grass, broadleaf weeds and sedges;
4. High safety to crops such as cotton, rape and paddy;
5. Having effective herbicidal activity to aged sensitive grass weeds (3 ~ 7 leaves)
6. Having short residual life in soil, have no adverse effect to rotational crops.
7. Having a favorable toxicological, ecotoxicological and environmental profile.

For practical use, the active compound of the present invention can be, according to usual formulation used in agricultural industry, formulated into various granule, powder, oil preparations, emulsions, aqueous suspensions or capsules.

The examples, for more detailed description of synthetic method, are given below. However, it is noted that the present invention is not limited to the range of the following examples.

Synthetic example 1: The preparation of compound (2) shown as formula (I) (R_1 = H)

Example:

9.3 g (0.1 mol) aniline is dissolved in 125 ml of anhydrous methanol. To this is added 12.2 g of (0.1 mol) salicylal dropwise. After stirred at room temperature for 10 minutes, the reaction mixture is filtered and the solid residue is washed with anhydrous methanol to give 18.0 g of yellow solid as the product. The yield for *N*-(2-hydroxybenzyl)-imine [corresponding to intermediate (5) in the previously described synthetic route] is 91.37 %.

9.85 g of the resulting *N*-(2-hydroxybenzyl)-imine (0.05 mol) is dissolved in 100 ml of anhydrous methanol. 1.29 g (0.034 mol) of sodium borohydride is added in portions. After the mixture is stirred at room temperature for 20 minutes, it is concentrated to remove methanol. 200 ml chloroform and 150 ml water are added to the residue. The mixture is well-stirred and then left to stand. The organic layer is separated, washed with water, dried over anhydrous sodium sulfate and concentrated to give 9.75 g of white solid as the product. The yield for *N*-(2-hydroxybenzyl)-aniline [corresponding to intermediate (5) in the previously described synthetic route] is 98.0 %.

1.99 g (10 mmol) *N*-(2-hydroxybenzyl)-aniline obtained from reaction above and 2.18 g (10 mmol) 2-methylsulfonyl-4,6-dimethoxypyrimidine are dissolved in 100 ml of tetrahydrofuran. To this is

added 3.71 g (26.84 mmol) of potassium carbonate at room temperature. The reaction mixture is refluxed for 11 hours, then suction filtered. The solid is extracted with 20 ml tetrahydrofuran. The mother liquid is concentrated. To the residue is added 10 ml ethanol, stirred and suction filtered to afford 3.00 g white solid as the product. The yield for *N*-phenyl-2-(4,6-dimethoxyprimidin-2-yloxy)-benzylamine is 89.0 %. M.p. 90.2 ~ 90.7 °C.

Elemental analysis: molecular formula $C_{19}H_{19}N_3O_3$ molecular weight 337

Calcd. C67.66 H5.64 N12.46 Found C67.70 H5.63 N12.55

NMR: HNMR ($CDCl_3$) δ (ppm) 3.81 (6H, s OCH_3), 4.33 (2H, s, CH_2), 5.77 (1H, s CH), 6.54~7.47 (9H, m, Ar-H)

Mass spectrum: Ms 337 (M^+)

Synthetic example 2: The preparation of compound shown as formula (I) ($R_1 \neq H$)

Example: In a 100 ml single-neck flask is added 0.89 g (2.64 mmol) *N*-phenyl-2-(4,6-dimethoxyprimidin-2-yloxy)-benzylamine, 0.82 g (7.25 mmol) chloroacetic acid chloride, 0.55 g (3.99 mmol) potassium carbonate and 30 ml THF. The mixture is refluxed for 10 hours. The solid is then removed by filtration. The organic layer is concentrated to afford 0.89 g waxy white solid, yield 77.7 %. M.p. 74.5 ~ 77.8 °C, as *N*-[phenyl-2-(4,6-dimethoxyprimidin-2-yloxy)-benzylamino]-2-chloroacetylphenylamine.

Elemental analysis: molecular formula $C_{21}H_{20}ClN_3O_4$ molecular weight 413

Calcd. C60.94 H4.84 N10.16 Found C60.88 H4.80 N10.31

NMR: HNMR ($CDCl_3$) δ (ppm) 3.77 (6H, s OCH_3), 4.13 (2H, s, CH_2), 5.01 (2H, s CH), 5.72 (1H, s, CH), 7.06~7.42 (9H, m, Ar-H)

MS: m/z 413 (M^+)

Next the examples of formulating several herbicide dosage forms are given, in which the compounds of the present invention are used as active ingredients. In these examples of formulations, all "%"refers to weight percent, "g ai/ha" refers to one gram active ingredients per hectare.

Formulation 1 (Wettable powder)

15 % compound No.70 (Table 1) is fully mixed with 5 % M_q,1 % JFC, 40 % diatomaceous earth and 44 % light calcium carbonate. Then the mixture is grinded and formulated as wettable powder.

Formulation 2 (Emulsifiable)

10 % compound No.70, 5 % emulsifier 500# and 5 % emulsifier 602# are dissolved in the solvent consisting of 5 % *N*-methyl-2-pyrrolidone and 75 % xylene by heating and stirring. The solution is formulated as emulsifiable.

Formulation 3 (Granule)

5 % compound No.70 (Table 1) is fully mixed with 1 % PVA, 4 % NMO and 90 % clay. The mixture is grinded and to 100 portions of this mixture is added 20 portions of water. After that, the mixture is kneaded and extruded the granules to formulate granule.

Next, the examples for conducting the test of biological activity and safety on the compounds of the present invention are given. It is noted that the present invention is not limited in the range of the following example.

The 5-grade evaluation criteria by visual examination for weeding activity and crop safety are listed in Table 2.

Table 2: The Evaluation Criteria for the phytotoxicity on weeds and crops by visual symptoms

Grade	Phytotoxocity (%)	Evaluation of activity on testing weeds by symptoms (suppression, deformity, whiten and etc.)	Evaluation of injury to crops (suppression, deformity, whiten and etc.)
0	0	same as CK, no activity, elimination	same as CK, tolerance, good
1	10-20	very slight activity, elimination	very slight, can be considered
2	30-40	Slight or moderate activity, elimination	slight, visual injury, elimination
3	50-60	moderate but unsufficient activity, can be further improved	more susceptible, heavy injury, elimination
4	70-80	good activity, can be considered,	very susceptible, heavy injury, elimination
5	90-100	better activity, good	very susceptible, heavy injury, elimination

Example 1: The results of phytotoxicity of post-emergency treatment (upland)

In the pots (9.5 cm diameter) containing testing soil, the seeds of *Echinochloa crusgalli*(ECHCG), *Digitaria sanguinalis*(DIGSA), *Eleusine indica*(ELEIN), *Brassica juncea*(BRAJU), *Amaranthus retroflexus*(AMARE) and *Portulaca oleracea*(POROL) are seeded, respectively and covered with

soil of 0.5 cm thick. The pots are placed into a greenhouse and incubate 10 days at 20 ~ 25℃. When the plants grow to two-leaf stage, the formulation obtained according to Formulation 2 is diluted with water, and conduct spraying on the plants incubated above in a dosage of 750 or 2250 g ai/ha. The visual injury of the individual plants is observed in regular intervals. The activity of the compounds is evaluated according to Table 2. The specific results are shown in Table 3.

Table 3: The evaluation of weed effects for post-emergency treatment (upland)

Compound No.	Dosage (g ai/ha)	The Evaluation Criteria for the phytotoxicity on weeds					
		ECHCG	DIGSA	ELEIN	BRAJU	AMARE	POROL
1	750	5	5	5	5	5	5
2	2250	5	5	5	5	5	5
3	2250	5	5	5	5	5	5
10	750	2	0	3	0	4	0
11	750	0	0	0	0	4	0
14	750	3	3	4	0	4	0
15	750	5	5	5	4	5	5
16	750	5	5	5	5	5	5
17	750	5	5	5	2	5	5
20	750	5	4	4	4	5	4
21	750	5	4	4	4	4	4
22	750	5	4	4	5	4	4
24	750	5	4	4	5	4	4
34	750	5	5	5	4	5	5
35	750	5	5	5	5	5	5
36	750	5	5	5	4	5	4
37	750	5	5	5	5	5	4
38	750	5	5	5	5	5	5
40	750	3	2	2	2	3	3
42	750	1	1	0	1	4	0
44	750	5	5	5	4	5	5
46	750	5	5	5	5	5	5
49	750	5	5	5	5	5	5
51	750	5	5	5	4	5	4
54	750	0	0	0	0	0	3
55	750	5	5	5	4	5	5
56	750	5	4	4	5	5	5

Example 2: The results of phytotoxicity activity of pre-emergency treatment

In the pots (9.5 cm diameter) containing testing soil, the seeds of *Echinochloa crusgalli*, *Digitaria sanguinalis*, *Eleusine indica*, *Brassica juncea*, *Amaranthus retroflexus* and *Portulaca oleracea* are seeded respectively, and covered with 0.5 cm thick soil. After 12 hours, the formulation obtained according to Formulation 2 is diluted with water, and conduct soil spraying treatment in a dosage of 750 or 2250 g ai/ha, which have planted the above seeds. The visual injury of the individual plants is observed in regular intervals. The phytotoxicity of the compounds is evaluated according to Table 2. The specific results are shown in Table 4.

Table 4: The evaluation for the phytotoxicity of pre-emergency treatment (upland)

Compound No.	Dosage (g ai/ha)	The evaluation criteria for the phytotoxicity on weeds					
		ECHCG	DIGSA	ELEIN	BRAJU	AMARE	POROL
1	750	4	4	5	4	5	5
2	2250	5	5	5	4	5	5
3	2250	5	5	5	4	5	5
10	750	0	0	2	0	2	0
11	750	0	0	0	0	0	0
14	750	0	0	3	0	0	0
15	750	4	5	5	2	5	5
16	750	5	4	5	3	5	5
17	750	3	4	4	2	5	5
20	750	3	4	4	4	5	4
21	750	3	4	4	4	5	4
22	750	4	4	5	4	5	4
24	750	4	4	4	5	5	4
34	750	4	4	4	5	5	5
35	750	5	5	5	5	5	5
36	750	4	5	4	5	5	5
37	750	5	5	5	5	5	5
38	750	5	5	5	5	5	5
40	750	1	2	2	3	3	3
42	750	0	0	0	0	1	1
44	750	4	5	5	5	5	5
46	750	4	4	5	5	5	5
49	750	5	5	5	5	5	5
51	750	3	3	3	5	5	5

54	750	0	0	0	0	0	0
55	750	4	5	5	5	5	5
56	750	5	5	5	4	5	5

Example 3: The effects of herbicidal compounds on testing weeds by gradient post-emergency treatment

The bio-tests with dosages in gradient are conducted by taking *Echinochloa crusgalli*, *Digitaria sanguinalis*, *Eleusine indica*, *Brassica juncea*, *Amaranthus retroflexus and Portulaca oleracea* as testing targets. When the grass weeds grow to two-leaf or broadleaf weeds grow to two-euphylla stage, they are spray treatment with Compound No. 3, 16 and 17 formulated according to Formulation 2 and diluted with water. The dosage treated to the test plant is listed in Table 5. The evaluation for the weeding activity according to Table 2 is made by 5-grade visual examination after 28 days, results listed in Table 5.

Table 5: The evaluation for phytotoxicity by gradient post-emergency treatment

Compound No.	Dosage (g ai/ha)	The Evaluation Criteria for the phytotoxicity on weeds					
		ECHCG	DIGSA	ELEIN	BRAJU	AMARE	POROL
3	375	5	5	5	4	5	4
	150	4	3	4	2	4	4
	75	2	0	3	4	4	4
16	375	5	5	4	5	5	4
	240	5	4	4	3	5	4
	124	4	4	4	3	5	2
17	375	5	5	5	4	5	5
	150	5	5	5	4	5	5
	75	5	4	4	2	5	4

Example 4: The evaluation for crop safety by post-emergency treatment

In pots (diameter of 12 cm) containing test soil, the cotton and rape seeds are planted respectively, and grown in a greenhouse at 20 ~ 25℃. After growing for the given period, the spraying treatment is conducted in 375, 150 and 75 g ai/ha dosages by diluting the formulation obtained according to Formulation 2 in water to a given concentration. The growing and visual injury status of the individual plants is observed in regular intervals after 28 days.

Table 6: Evaluation for crops safety of post-emergency treatment (upland)

Compound No.	Dosage (g ai/ha)	Evaluation for crops safety	
		Rape	Cotton
2	375	1	0
	150	0	0
	75	0	0
3	375	1	0
	150	0	0
	75	0	0
17	375	1	0
	150	0	0
	75	0	0

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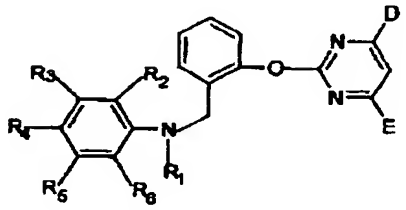
权利要求书3页 说明书16页 附图页数0页

[54]发明名称 2－嘧啶氧基苄基取代苯基胺类衍生物

[57]摘要

一类如结构式(I)所示2－嘧啶氧基苄基取代苯基胺类衍生物，系由取代苯胺和水杨醛 反应，所得中间体经还原后再与2－甲砜基－4,6－取代嘧啶反应制得如结构式(I)所示(R_1 = H) 的化合物，该化合物再与酰氯反应制得如结构式(I)所示($R_1 \neq H$)的化合物。结构式(I) 所示的胺类衍生物具有很好的除草活性，适用于配制棉花、油菜、小麦田除草剂，它们的 防治效果好，用量低，除草谱广，低毒，不伤害作物，对环境友好。



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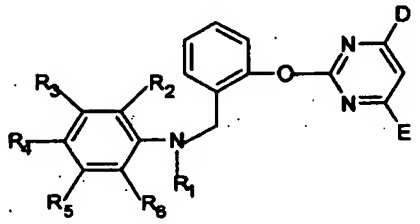
1、一类嘧啶类化合物，其特征是 2-嘧啶氧基苄基取代苯基胺类衍生物，如结构式（I）所示：



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结构式（I）中：

D 和 E 可以是相同的或不同的基团，分别为氢、卤素、C_1—C_4烷基、C_1—C_4烷氧基或C_1—C_4卤代烷基；

R_1为氢、C_1—C_4烷酰基、C_1—C_4卤代烷酰基、苯酰基或C_1—C_4烷氧乙酰基；

R_2为氢、卤素、C_1—C_4烷基或三氟甲基；

R_3为氢、卤素、C_1—C_4烷基、三氟甲基、硝基或氰基；

R_4为氢、卤素、C_1—C_4烷基、C_1—C_4烷氧基、C_1—C_4烷酯基、三氟甲基、氰基、羧基或其碱金属盐、碱土金属盐、过渡金属盐或有机铵盐；

R_5为氢或卤素；

R_6为氢、卤素或C_1—C_4烷基。

2、根据权利要求 1 所述结构式（I）2-嘧啶氧基苄基取代苯基胺类衍生物，其特征是结构式（I）中 D 和 E 均为甲氧基，或其中之一为甲氧基，另一个为氯或甲基；R_1为氢、乙酰基、氯乙酰基、二氯乙酰基、苯酰基或甲氧乙酰基；R_2为氢、氟、氯、溴、碘、甲基、乙基或三氟甲基；R_3为氢、氯、氟、甲基、三氟甲基、硝基或氰基；R_4为氢、氟、氯、溴、碘、甲基、三氟甲基、甲氧基、C_1—C_4烷酯基、羧基或其钠盐或钾盐；R_5为氢或氯；R_6为氢、甲基或乙基。

3、根据权利要求 1 或 2 所述 2-嘧啶氧基苄基取代苯基胺类衍生物，其特征是结构式（I）中 D 和 E 均为甲氧基；R_1为氢。

4、根据权利要求 1、2 或 3 所述 2-嘧啶氧基苄基取代苯基胺类衍生物的制备方法，其特征如下列反应方程式所表示：

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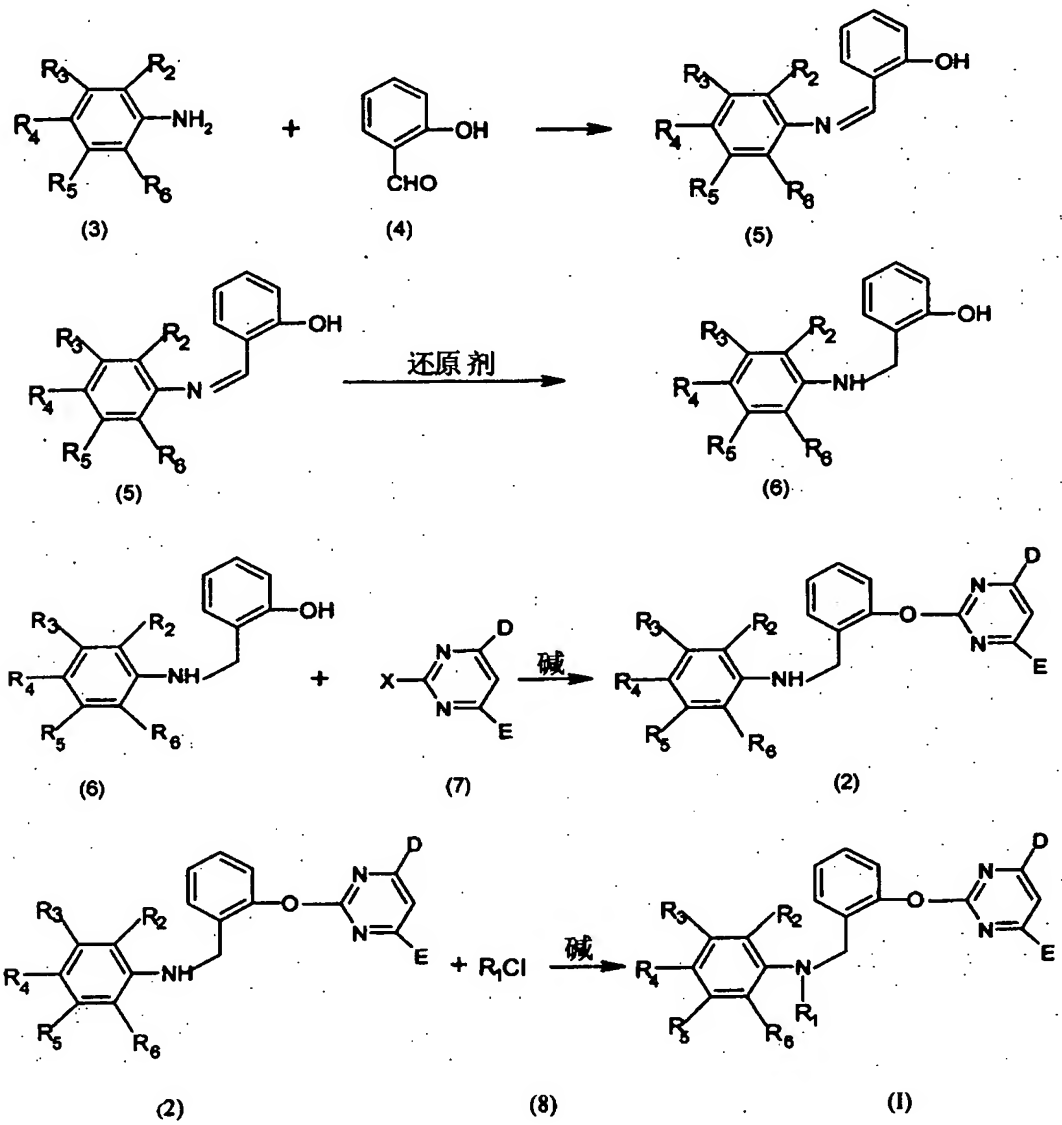

（反应式中各取代基所代表基团如权利要求 1、2 或 3 所述，$R_1 \neq H$，X 为卤素或甲砜基）

首先由取代苯胺（3）和水杨醛（4）以 1:1.0-1.2 的摩尔比溶于醇溶剂中，在室温至溶剂沸点温度区间反应 20—60 分钟，得到中间体（5），再在醇溶剂中加入硼氢化钠或硼氢化钾还原后得中间体（6），除去溶剂后与 2-卤代-4,6-取代嘧啶或 2-甲砜基-4,6-取代嘧啶（7）（4，6-取代基即为权利要求 1 所述 D 和 E 取代基）以 1:1.0-1.1 摩尔比在醚类溶剂和碱性条件下反应，即制得如结构式（I）所示（R_1=H）的化合物（2），该类化合物（2）再与酰氯（8）进一步在醚类溶剂中并在碱性条件下反应，即制得如结构式（I）所示（$R_1 \neq H$）的化合物。

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5、 根据权利要求 1、2 或 3 所述 2-嘧啶氧基苄基取代苯基胺类衍生物，其特征是有很高的除草活性，可用于配制农作物棉花、油菜和小麦田防除禾本科杂草、阔叶杂草和莎草的芽前、芽后除草剂。

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说 明 书

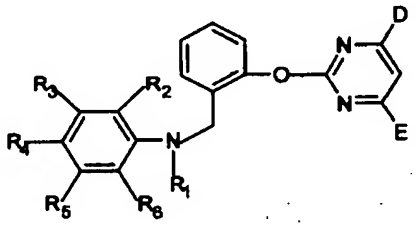
2-嘧啶氧基苄基取代苯基胺类衍生物

本发明涉及嘧啶类化合物，特别是 2-嘧啶氧基苄基取代苯基胺类衍生物，它们的制备方法及其作为农业化学品除草剂的配方和应用。

当今，农业现代化的发展，需要不断提供效果好，用量低，对作物和环境无害的新型除草剂，以减少农业劳动力，促进农业机械化、现代化发展和作物产量的提高。

已知各种 2-苯氧基嘧啶衍生物作为除草剂是有效的，如美国专利 4,906,285 阐述了双嘧啶水杨酸类化合物具有广谱的除草范围，而美国专利 4,932,999 则揭示了嘧啶硫代水杨酸衍生物对多年生及一年生草类显示出优异的除草效果。但它们仅适用于棉花田和水稻田的除草，它们对油菜会有不同程度的损害。

基于社会发展的需要，并为扩大使用范围，开发同时适用于油菜田的除草剂，本发明人在已有发明的基础上，进行先导展开，开发出了如结构式（I）所示一类 2-嘧啶氧基苄基取代苯基胺类衍生物。



（I）

式（I）中：

D 和 E 可以是相同的或不同的基团，分别为氢、卤素、C_1—C_4烷基、C_1—C_4烷氧基或 C_1—C_4卤代烷基，其中更可取的是 D 和 E 均为甲氧基，或其中之一为甲氧基，另一个为氯或甲基，特别可取的是 D 和 E 均为甲氧基；

R_1为氢、C_1—C_4烷酰基、C_1—C_4卤代烷酰基、苯酰基或 C_1—C_4烷氧乙酰基，其中较为可取的是氢、乙酰基、氯乙酰基、二氯乙酰基、苯酰基或甲氧乙酰基，更为可取的是氢、氯乙酰基或甲氧乙酰基，特别可取的是氢。

R_2为氢、卤素、C_1—C_4烷基或三氟甲基，其中更可取的是氢、氟、氯、溴、碘、甲基、乙基或三氟甲基；

R_3为氢、卤素、C_1—C_4烷基、三氟甲基、硝基或氰基，其中更为可取的是氢、氟、氯、

甲基、三氟甲基、硝基或氰基；

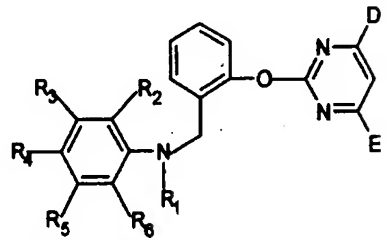
R_4为氢、卤素、C_1—C_4烷基、C_1—C_4烷氧基、C_1—C_4烷酯基、三氟甲基、氰基、羧基或其碱金属盐、碱土金属盐、过渡金属盐或有机铵盐，其中更为可取的是氢、氟、氯、溴、碘、甲基、三氟甲基、甲氧基、C_1—C_4烷酯基、羧基或其钠盐、钾盐或铵盐。

R_5为氢或卤素，更可取的是氢或氯；

R_6为氢、卤素或C_1—C_4烷基，更可取的是氢、甲基或乙基。

本发明人，通过分子设计，改变结构式（I）中D和E及从R_1到R_6各取代基及其不同的组合，合成出了一系列化合物，并由生测专家对其进行除草活性和毒性的测定评价，其中已筛选出一批有较高除草活性的化合物，这些化合物归总列表于1。

表 1



编号	D	E	R_1	R_2	R_3	R_4	R_5	R_6	元素分析（%）			质谱
									C	H	N	M^+
1	OCH_3	OCH_3	H	H	H	Br	H	H	54.68	4.30	10.20	415
2	OCH_3	OCH_3	H	H	H	I	H	H	49.11	3.86	9.00	463
3	OCH_3	OCH_3	H	H	H	$CO_2(CH_2)_2CH_3$	H	H	65.10	5.88	9.99	423
4	OCH_3	OCH_3	H	H	H	OCH_3	H	H	65.33	5.75	11.25	367
5	OCH_3	OCH_3	$COCH_2Cl$	H	H	$CO_2(CH_2)_2CH_3$	H	H	60.21	5.28	8.30	499
6	OCH_3	OCH_3	$COCH_2Cl$	H	H	OCH_3	H	H	59.25	4.99	9.40	443
7	OCH_3	OCH_3	$COCH_2CH_3$	H	H	I	H	H	50.70	4.28	8.21	519
8	OCH_3	OCH_3	$COCH_3$	H	H	I	H	H	49.88	4.00	8.11	505
9	OCH_3	OCH_3	$CO(CH_2)_3Cl$	H	H	Br	H	H	53.11	4.50	8.10	519
10	OCH_3	OCH_3	COPh	H	H	Br	H	H	60.01	4.28	8.09	519
11	OCH_3	OCH_3	$COCHCl_2$	H	H	Br	H	H	47.77	3.47	7.97	527
12	OCH_3	OCH_3	$COCH_2CH_3$	H	H	Br	H	H	55.81	4.65	8.72	471
13	OCH_3	OCH_3	$COCH_2Cl$	H	H	Br	H	H	51.22	3.89	8.44	491

续表 1

编号	D	E	R_1	R_2	R_3	R_4	R_5	R_6	元素分析（%）			质谱
									C	H	N	M^+
14	OCH_3	OCH_3	$COCHCl_2$	H	H	OCH_3	H	H	55.00	4.40	8.66	477
15	OCH_3	OCH_3	$CO(CH_2)_3Cl$	H	H	OCH_3	H	H	61.12	5.60	8.78	471
16	OCH_3	OCH_3	H	Cl	H	H	Cl	H	56.30	4.22	10.33	405
17	OCH_3	OCH_3	H	CH_3	H	H	Cl	H	62.07	5.25	10.88	385
18	OCH_3	OCH_3	$COCH_2Cl$	Cl	H	H	Cl	H	52.11	3.71	8.56	481
19	OCH_3	OCH_3	$COCH_2Cl$	CH_3	H	Cl	H	H	57.25	4.59	9.20	461
20	OCH_3	OCH_3	H	F	H	H	H	H	64.09	5.10	11.88	355
21	OCH_3	OCH_3	H	Cl	H	H	H	H	61.21	4.86	11.54	371
22	OCH_3	OCH_3	H	H	H	Cl	H	H	61.29	4.89	11.33	371
23	OCH_3	OCH_3	H	Cl	Cl	H	H	H	56.30	4.21	10.50	405
24	OCH_3	OCH_3	H	H	H	CH_3	H	H	68.25	5.99	11.88	351
25	OCH_3	OCH_3	H	H	Cl	Cl	H	H	56.06	4.14	10.44	405
26	OCH_3	OCH_3	H	H	Cl	H	H	H	61.50	4.86	11.50	371
27	OCH_3	OCH_3	$COCH_2Cl$	F	H	H	H	H	58.28	4.35	9.66	431
28	OCH_3	OCH_3	$COCH_2Cl$	Cl	H	H	H	H	56.21	4.30	9.50	447
29	OCH_3	OCH_3	$COCH_2Cl$	H	H	Cl	H	H	56.20	4.21	9.52	447
30	OCH_3	OCH_3	$COCH_2Cl$	Cl	Cl	H	H	H	52.17	3.75	8.56	481
31	OCH_3	OCH_3	$COCH_2Cl$	H	H	CH_3	H	H	61.68	5.20	9.87	427

续表 1

编号	D	E	R_1	R_2	R_3	R_4	R_5	R_6	元素分析（%）			质谱
									C	H	N	M^+
32	OCH_3	OCH_3	$COCH_2Cl$	H	Cl	Cl	H	H	52.15	3.80	8.55	481
33	OCH_3	OCH_3	$COCH_2Cl$	H	Cl	H	H	H	56.18	4.30	9.39	447
34	OCH_3	OCH_3	H	CH_3	Cl	H	H	H	62.22	5.25	10.79	385
35	OCH_3	OCH_3	H	CH_3	H	H	H	H	68.25	5.89	11.88	351
36	OCH_3	OCH_3	H	H	Cl	H	Cl	H	56.22	4.14	10.45	405
37	OCH_3	OCH_3	H	Cl	H	Cl	H	H	56.09	4.17	10.33	405
38	OCH_3	OCH_3	H	CH_3	H	CH_3	H	H	69.01	6.35	11.64	365
39	OCH_3	OCH_3	$COCH_2Cl$	CH_3	H	H	H	H	61.76	5.21	9.78	427
40	OCH_3	OCH_3	$COCH_2Cl$	H	Cl	H	Cl	H	52.33	3.69	8.79	481
41	OCH_3	OCH_3	$COCH_2Cl$	Cl	H	Cl	H	H	52.40	3.77	8.55	481
42	OCH_3	OCH_3	$COCH_2Cl$	CH_3	H	CH_3	H	H	62.45	5.49	9.70	441
43	OCH_3	OCH_3	$COCH_2Cl$	CH_3	H	H	H	CH_3	62.60	5.41	9.66	441
44	OCH_3	OCH_3	H	CF_3	H	H	H	H	59.33	4.48	10.45	405
45	OCH_3	OCH_3	$COCH_2Cl$	CF_3	H	H	H	H	54.90	4.01	8.88	481
46	OCH_3	OCH_3	H	H	H	CF_3	H	H	59.27	4.40	10.30	405
47	OCH_3	OCH_3	$COCH_2Cl$	H	H	CF_3	H	H	54.79	3.99	8.56	481
48	OCH_3	OCH_3	$COCH_2Cl$	H	H	I	H	H	46.80	3.54	7.88	539
49	OCH_3	OCH_3	H	H	F	H	H	H	64.33	5.11	11.77	355

续表 1

编号	D	E	R_1	R_2	R_3	R_4	R_5	R_6	元素分析（%）			质谱
									C	H	N	M^+
50	OCH_3	OCH_3	$COCH_2Cl$	H	F	H	H	H	58.29	4.35	9.90	431
51	OCH_3	OCH_3	H	H	I	H	H	H	49.25	3.85	9.11	463
52	OCH_3	OCH_3	$COCH_2Cl$	H	I	H	H	H	46.66	3.59	7.79	539
53	OCH_3	OCH_3	H	H	CH_3	CH_3	H	H	69.20	6.35	11.56	365
54	OCH_3	OCH_3	$COCH_2OCH_3$	H	H	Cl	H	H	59.36	4.90	9.40	443
55	OCH_3	OCH_3	H	H	CF_3	H	H	Cl	54.53	3.81	9.66	439
56	OCH_3	OCH_3	H	C_2H_5	H	H	H	C_2H_5	70.15	6.82	10.78	393
57	OCH_3	OCH_3	H	I	H	H	H	H	49.19	3.80	9.14	463
58	OCH_3	OCH_3	$COCH_2OCH_3$	H	F	H	H	H	61.68	5.10	9.69	427
59	OCH_3	OCH_3	$COCH_2OCH_3$	H	H	I	H	H	49.20	4.14	7.72	535
60	OCH_3	OCH_3	$COCH_2OCH_3$	H	Cl	Cl	H	H	55.26	4.35	8.88	477
61	OCH_3	OCH_3	$COCH_2Cl$	H	CH_3	CH_3	H	H	62.55	5.40	9.60	441
62	OCH_3	OCH_3	$COCH_2Cl$	C_2H_5	H	H	H	C_2H_5	63.89	5.97	8.99	469
63	OCH_3	OCH_3	$COCH_2Cl$	H	CF_3	H	H	Cl	51.30	3.43	8.15	515
64	OCH_3	OCH_3	$COCH_2Cl$	I	H	H	H	H	46.88	3.53	7.78	539
65	OCH_3	OCH_3	$COCH_2OCH_3$	H	Cl	H	H	H	59.45	4.91	9.50	443
66	OCH_3	OCH_3	$COCH_2OCH_3$	H	I	H	H	H	49.50	4.17	7.85	535
67	OCH_3	OCH_3	H	H	H	H	H	H	67.70	5.63	12.55	337

续表 1

编号	D	E	R_1	R_2	R_3	R_4	R_5	R_6	元素分析（%）			质谱
									C	H	N	M^+
68	OCH_3	OCH_3	H	CH_3	H	Br	H	H	55.68	4.70	9.92	429
69	OCH_3	OCH_3	H	Br	H	H	H	H	54.77	4.41	10.20	415
70	OCH_3	OCH_3	H	H	H	F	H	H	64.40	5.10	11.89	355
71	OCH_3	OCH_3	H	H	CF_3	H	H	H	59.29	4.50	10.34	405
72	OCH_3	OCH_3	H	H	Cl	F	H	H	58.44	4.31	10.77	389
73	OCH_3	OCH_3	H	CH_3	NO_2	H	H	H	60.49	5.10	14.30	395
74	OCH_3	OCH_3	H	H	NO_2	CH_3	H	H	60.56	5.08	14.20	395
75	OCH_3	OCH_3	$COCH_2Cl$	H	H	H	H	H	60.88	4.80	10.16	413
76	OCH_3	OCH_3	H	H	H	CN	H	H	66.21	4.94	15.44	362
77	OCH_3	OCH_3	H	H	CN	H	H	H	66.29	4.99	15.56	362
78	OCH_3	OCH_3	H	H	H	CO_2CH_3	H	H	63.77	5.25	10.70	395
79	OCH_3	OCH_3	H	H	H	$CO_2C_2H_5$	H	H	64.45	5.60	10.41	409
80	OCH_3	OCH_3	H	H	H	$CO_2C_4H_9$-n	H	H	65.88	6.21	9.56	437
81	OCH_3	OCH_3	H	H	H	$CO_2CH(CH_3)_2$	H	H	65.33	5.88	9.78	423
82	OCH_3	OCH_3	H	H	H	CO_2Na	H	H	59.65	4.52	10.45	403
83	OCH_3	OCH_3	H	H	H	CO_2K	H	H	57.41	4.26	10.11	419
84	OCH_3	OCH_3	H	H	H	CO_2H	H	H	62.79	4.89	11.20	381
85	Cl	OCH_3	H	H	H	$CO_2C_2H_5$	H	H	60.88	4.80	10.31	413

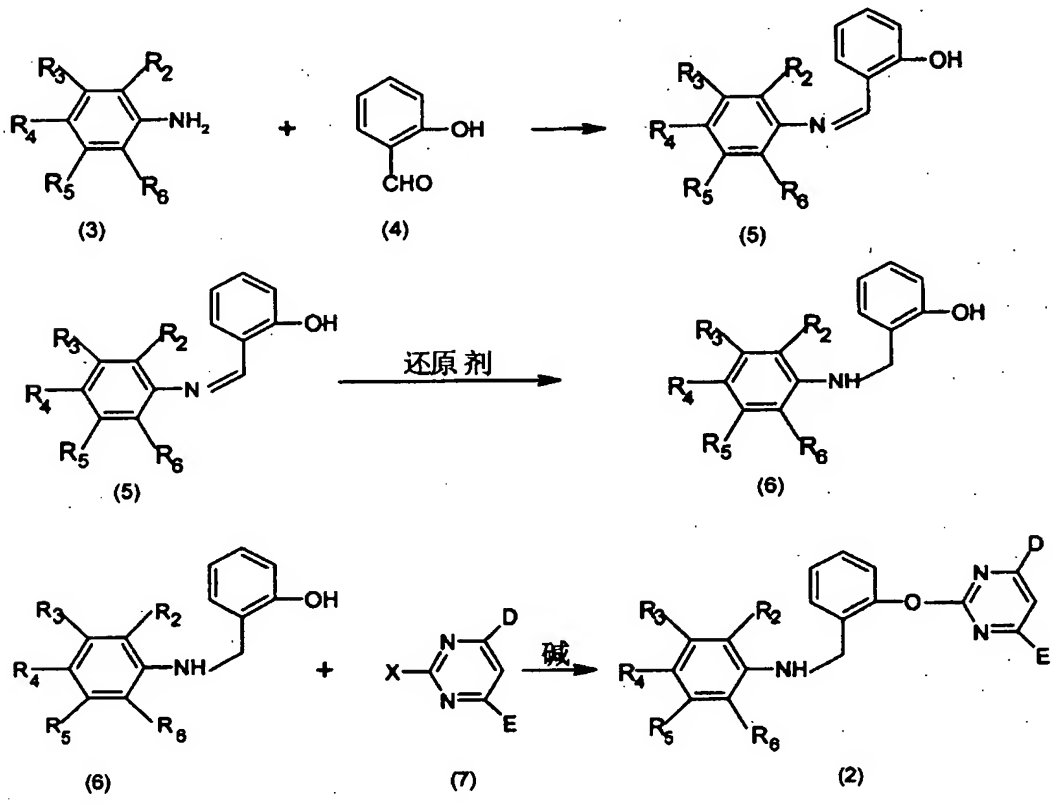
续表 1

编号	D	E	R_1	R_2	R_3	R_4	R_5	R_6	元素分析（%）			质谱
									C	H	N	M^+
86	CH3	OCH_3	H	H	H	$CO_2C_2H_5$	H	H	67.30	5.81	10.59	393
87	OCH_3	OCH_3	H	H	H	$CO_2H•NH(CH_3)_2$	H	H	61.99	6.19	13.25	381

生测表明，结构式（I）所示 2-嘧啶氧基苄基取代苯基胺类衍生物具有很好的除草活性，而且除草谱广，低毒，对环境友好，不伤害作物。因此，它们是配制农用除草剂的有效活性物。

本发明化合物品种很多，但结构式相似，属同系列化合物，因而，其合成方法亦基本相似。本发明人所采用的合成方法如下：

A、结构式（I）所示（R_1=H）的化合物合成方法，分三步，可以反应方程式表示如下：



上述反应式中各化合物中的 R_2、R_3、R_4、R_5、R_6 及 D、E 所代表的取代基，如前所述，X 为卤素或甲砜基。

也就是说，本发明结构式（I）所示（R_1=H）的化合物（2）的合成，首先由取代苯胺（3）和水杨醛（4）以 1:1.0-1.2 的摩尔比溶于甲醇、乙醇或丙醇类醇溶剂中，在室温至溶剂沸点的温度区间内反应 20—60 分钟，得到中间体（5）。反应可在无催化剂的情况下进行，而加入催化剂和在共沸脱水的情况下，可以加快反应，提高反应收率。反应中所用的催化剂可以是对甲基苯磺酸、甲磺酸、硫酸或盐酸。

反应中所用溶剂除醇类溶剂外，还可用芳烃，如苯、甲苯或二甲苯；卤代烃，如二氯甲烷、二氯乙烷或氯仿；醚溶剂，如四氢呋喃或二氧六环；酮溶剂，如丙酮或甲基异丁基酮；或二甲基甲酰胺或二甲基亚砜；或乙腈及它们的混合物。

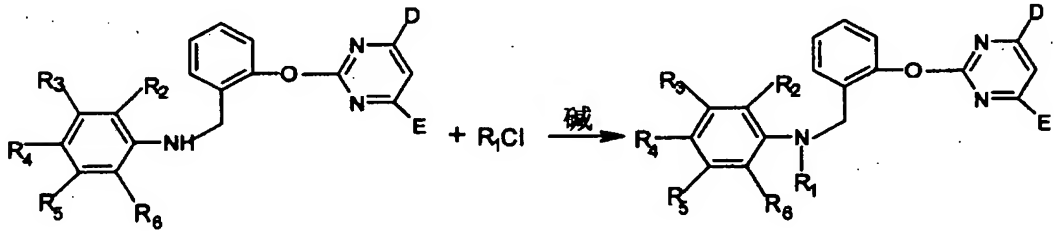
然后，将第一步所得的中间体（5）在甲醇、乙醇或丙醇类溶剂中，在硼氢化钠或硼氢化钾还原剂存在下在室温还原反应得中间体（6）。

第三步，使中间体（6）和 2-卤代-4,6-取代嘧啶或 2-甲砜基-4,6-取代嘧啶（7）以 1:1.0-1.2 摩尔比在溶剂中并在碱存在的条件下反应，即得本发明的产物如结构式（I）所示（R_1=H）的化合物（2）。在这一步反应中，所用碱可以是金属钠或钾之类碱金属，或氢化钠、氢化钾之类碱金属氢化物，或氢化钙之类碱土金属化合物，或醇钠、醇钾之类烷氧金属化合物，或碳酸钠、碳酸钾之类碱金属碳酸盐，或三乙胺、吡啶等有机胺。

在第三步反应中所用的溶剂，可以是苯、甲苯或二甲苯等芳烃溶剂，甲醇、乙醇、丙醇等醇溶剂，四氢呋喃、二氧六环等醚类溶剂，丙酮、甲基异丁酮等酮类溶剂，二甲基甲酰胺、二甲基亚砜等溶剂，或乙腈及它们的混合物。

（B）结构式（I）所示（R_1≠H）的化合物的合成方法：

如前所述，经过三步反应所得如结构式（I）所示（R_1=H）的化合物（2），即是我们所需要的具有除草功能的活性物之一，而若将其与酰氯（8）进一步在溶剂中并在碱存在的条件下反应，还可得到同样具有除草活性的如结构式（I）所示（R_1≠H）的化合物，反应可以用下列反应式表示：



(2)　　(8)　　(I)

反应式中 D 和 E、R_1-R_6 均如前所述（R_1≠H）。

本反应的温度在室温到溶剂沸点温度区间，反应所用溶剂和碱与前述如结构式（I）所示（R_1=H）的化合物（2）合成第三步相同。

本发明 2-嘧啶氧基苄基取代苯基胺类衍生物，合成方法不复杂，产品均具有很好的除草活性，是配制农用除草剂的有效活性物质。

本发明提供的式(I)化合物及其制剂能有效地防治大多数农田杂草，45-75g ai/ha(g ai/ha 为克活性物/公顷，以下同)的低剂量下有效防治禾本科杂草、150-300 g ai/ha 高剂量下有效防治阔叶杂草和莎草，如稗草（*Echinochloa crusgalli*）、马唐（*Digitaria sanguinalis*）、牛筋草（*Eleusine indica*）、狗尾草（*Setaria viridis*）、早熟禾（*Poa annua*）、野燕麦（*Avena fatua*）、

看麦娘（*Alopecurus aequalis*）、日本看麦娘（*Alopecurus japonicus*）、反枝苋（*Amaranthus retroflexus*）、刺苋（*Amaranthus spinosus*）、藜（*Chenopodium album*）、芥菜（*Brassica juncea*）、马齿苋（*Portulaca oleracea*）、铁苋菜（*Acalypha australis*）、异型莎草（*Cyperus difformis*）、千金子（*Leptochloa chinensis*）、香附子（*Cyperus rotundus*）、日照飘浮草（*Fimbristylis miliacea*）、婆婆纳（*Veronica didyma*）、繁缕（*Stallaria media*）、大巢菜（*Vicia sativa*）、雀舌草（*Stellaria alsine*）、一年蓬（*Erigeron annuus*）、矮慈姑（*Sagittaria sagittifolia*）、田旋花（*Convolvulus arvensis*）等。作为除草剂，它们具有如下一些优点和特点：

1、除草活性高，低剂量用量亦有效；

2、低剂量下具有高效的芽后除草效果，较高剂量下亦具芽前除草效果；

3、杀草谱广，不仅能有效防除农田中禾本科杂草，而且能防除阔叶杂草和莎草；

4、对作物的安全性高，物别对棉花、油菜、水稻非常安全；

5、对 3—7 叶大龄禾本科杂草也具有十分有效的除草活性；

6、在土壤中残留期短，对轮作后茬作物生长无不良影响；

7、对哺乳动物或鱼无明显毒性，环境安全性高，属低毒环境友好型农药；

为实际使用，本发明活性化合物，可按农药工业中常用配方技术，配制加工成各种粒剂、粉剂、油剂、乳剂、水悬剂或胶囊剂等。

以下举实施例，对本发明合成方法作更进一步具体描述，但应申明，本发明决不限于此具体例。

合成例 1：结构式（I）所示（R_1=H）的化合物（2）的制备

实例：将 9.3 克（0.1 摩尔） 苯胺溶于 125 毫升的无水甲醇 中，滴加 12.2 克（0.1 摩尔）水杨醛，在室温下搅拌反应 10 分钟后，过滤，固体用无水甲醇洗涤，得 18.0 克黄色固体产物，收率 91.37%，为 N-(2-羟基亚苄基）苯胺[相当于前述合成方法中的中间体(5)]。

取上述所制 N-(2-羟基亚苄基）苯胺 9.85 克（0.05 摩尔），溶于 100 毫升无水甲醇中，在室温下分批加入 1.29 克（0.034 摩尔）硼氢化钠，室温下搅拌反应 20 分钟，浓缩除去甲醇，然后在残留物中加入氯仿 200 毫升，水 150 毫升，充分搅拌均匀，静置，分出有机层，用水洗涤，无水硫酸钠干燥，浓缩得 9.75 克白色固体产物，收率 98.0%，为 N-(2-羟基苄基）苯胺[相当于前述合成方法中的中间体（6）。

取上面所制 N-(2-羟基苄基）苯胺 1.99 克（10 毫摩尔），2-甲砜基-4,6-二甲氧基嘧啶 2.18 克（10 毫摩尔），溶于 100 毫升四氢呋喃中，室温下加入 3.71 克（26.84 毫摩尔）碳酸钾，

回流反应 11 小时，抽滤，固体用 20 毫升四氢呋喃洗涤，母液浓缩，残留产物加入 10 毫升乙醇搅拌洗涤，抽滤得 3.00 克白色固体产物，收率 89.0%，mp90.2-90.7℃，为 N-苯基-2-(4,6-二甲氧基嘧啶-2-基)氧基苯胺。

元素分析：分子式 $C_{19}H_{19}N_3O_3$ 分子量 337

理论值 C67.66 H5.64 N12.46 实测值 C67.70 H5.63 N12.55

核磁共振：HNMR（$CDCl_3$）δ（ppm）3.81(6H,s,OCH_3),4.33(2H,s,CH_2),5.77(1H,s,CH),6.54-7.47(9H,m,Ar-H)

质 谱：Ms 337(M^+)

合成例 2：结构式（I）所示（$R_1 \neq H$）的化合物制备

实例：在 100 毫升单口瓶中，加入 N-苯基-2-(4,6-二甲氧基嘧啶-2-基)氧苯苄胺 0.89 克（2.64 毫摩尔），氯乙酰氯 0.82 克（7.25 毫摩尔），碳酸钾 0.55 克（3.99 毫摩尔）及 30 毫升 THF，回流反应 10 小时，抽滤，除去固体，有机层浓缩得蜡状白色固体 0.89 克，收率 77.7%，mp74.5-77.8℃，为 N-[2-(4,6-二甲氧基嘧啶-2-基)氧基苄胺基]-2-氯代乙酰基苯胺。

元素分析：分子式 $C_{21}H_{20}ClN_3O_4$ 分子量 413

理论值 C60.94 H4.84 N10.16 实测值 C60.88 H4.80 N10.31

核磁共振：HNMR（$CDCl_3$）δ（ppm）3.77(6H ,s,OCH_3),4.13(2H,s,CH_2), 5.01(2H,s,CH_2), 5.72(1H,s,CH),7.06-7.42(9H,m,Ar-H)。

质 谱：Ms 413(M^+)

以下给出以本发明化合物作活性物质组份，加工配制几种除草剂剂型的实际例子，在这些配方例子中，所有的“%”均指重量百分比，“g ai/ha” 均指克活性物/公顷。

配方例 1（可湿性粉剂）

将 15%的 70 号物质（表 1）、5%的木质素磺酸盐（M_q）、1%的月桂醇聚氧乙烯醚（JFC）、40%的硅藻土和 44%的轻质碳酸钙均匀地混合，粉碎，即得可湿性粉剂。

配方例 2（乳油）

将 10%的 70 号物质、5%的农乳 500 号（钙盐）、5%的农乳 602 号、5%的 N-甲基-2-吡咯烷酮和 75%的二甲苯加热搅拌均匀，即得乳油。

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配方例 3（粒剂）

将 5%的 70 号物质（表 1）、1%的聚乙烯醇（PVA）、4%的萘磺酸钠甲醛缩合物(NMO)和 90%粘土均匀地混合，粉碎，然后向此 100 份混合物加入 20 份水、捏合，用挤压成粒机，制成 14—32 目的颗粒，干燥，即得颗粒剂。

以下将通过生测专家提供的生测试验实例对本发明部分化合物作活性组分配制的除草剂的除草活性和作物安全性进行测试评价。评价标准列于表 2。

表 2：除草活性和植物毒性评价标准

分级指数	植物毒性（%）	除草活性评语（抑制、畸形、白化等）	作物安全性评语（抑制、畸形、白化等）
0	0	同对照，耐，淘汰	同对照，耐，正常
1	10-20	轻，稍有影响，淘汰	轻，稍有影响，可考虑
2	30-40	轻，有影响，淘汰	敏感，有影响，淘汰
3	50-60	敏感，有影响，可考虑进一步改造	较敏感，药害重，淘汰
4	79-80	较敏感，可考虑	极敏感，药害重，淘汰
5	90-100	极敏感，好	极敏感，药害重，淘汰

试验实例 1：苗后茎叶处理的除草活性试验

在装有试验用土的盆钵中（直径 9.5cm）分别均匀地播种稗、马唐、牛筋、芥菜、反枝苋和马齿苋的种子，覆盖土 0.5cm 厚，将盆钵置于 20-25℃的温室中培育 10 天。植株生长二叶期时，将类似配方例 2 所制备的各号活性物乳油制剂用水稀释，以 2250g ai/ha 或 750g ai/ha 的剂量对培养试材进行茎叶喷雾处理。定期观察各处理植株生长状态、受害症状，处理后 28 天，按照表 2 中确定的标准进行评定。结果见表 3。

表 3：出苗后叶面处理的除草活性（旱田条件）

化合物编号	剂量（g ai/ha）	除草活性指数					
		稗草	马唐	牛筋草	芥菜	反枝苋	马齿苋
1	750	5	5	5	5	5	5
2	2250	5	5	5	5	5	5
3	2250	5	5	5	5	5	5
10	750	2	0	3	0	4	0
11	750	0	0	0	0	4	0
14	750	3	3	4	0	4	0
15	750	5	5	5	4	5	5

续表 3

化合物编号	剂量（g ai/ha）	除草活性指数					
		稗草	马唐	牛筋草	芥菜	反枝苋	马齿苋
16	750	5	5	5	5	5	5
17	750	5	5	5	2	5	5
20	750	5	4	4	4	5	4
21	750	5	4	4	4	4	4
22	750	5	4	4	5	4	4
24	750	5	4	4	5	4	4
34	750	5	5	5	4	5	5
35	750	5	5	5	5	5	5
36	750	5	5	5	4	5	4
37	750	5	5	5	5	5	4
38	750	5	5	5	5	5	5
40	750	3	2	2	2	3	3
42	750	1	1	0	1	4	0
44	750	5	5	5	4	5	5
46	750	5	5	5	5	5	5
49	750	5	5	5	5	5	5
51	750	5	5	5	4	5	4
54	750	0	0	0	0	0	3
55	750	5	5	5	4	5	5
56	750	5	4	4	5	5	5

试验实例 2：苗前土壤处理的除草活性试验

在装有试验用土的盆钵中(直径 9.5cm)分别均匀播种稗、马唐、牛筋、芥菜、反枝苋和马齿苋的种子，覆盖土 0.5cm 厚，12 小时后将类似配方例 2 所制备的各号活性物乳油制剂用水稀释，并以 2250 或 750g ai/ha 的剂量对培养试材进行土壤表面处理。定期观察各处理植株生长状态、受害症状，处理后 28 天，按照表 2 中确定的标准进行评定，结果见表 4。

表 4：出苗前土壤处理的除草活性(旱地条件)

化合物编号	剂量 (g ai/ha)	除草活性指数					
		稗草	马唐	牛筋草	芥菜	反枝苋	马齿苋
1	750	4	4	5	4	5	5
2	2250	5	5	5	4	5	5

续表 4

化合物编号	剂量 (g ai/ha)	除草活性指数					
		稗草	马唐	牛筋草	芥菜	反枝苋	马齿苋
3	2250	5	5	5	4	5	5
10	750	0	0	2	0	2	0
11	750	0	0	0	0	0	0
14	750	0	0	3	0	0	0
15	750	4	5	5	2	5	5
16	750	5	4	5	3	5	5
17	750	3	4	4	2	5	5
20	750	3	4	4	4	5	4
21	750	3	4	4	4	5	4
22	750	4	4	5	4	5	4
24	750	4	4	4	5	5	4
34	750	4	4	4	5	5	5
35	750	5	5	5	5	5	5
36	750	4	5	4	5	5	5
37	750	5	5	5	5	5	5
38	750	5	5	5	5	5	5
40	750	1	2	2	3	3	3
42	750	0	0	0	0	1	1
44	750	4	5	5	5	5	5
46	750	4	4	5	5	5	5
49	750	5	5	5	5	5	5
51	750	3	3	3	5	5	5
54	750	0	0	0	0	0	0
55	750	4	5	5	5	5	5
56	750	5	5	5	4	5	5

试验实例 3：苗后茎叶处理的除草活性剂量梯度试验

以稗草、马唐、牛筋、芥菜、反枝苋和马齿苋为杂草靶标，进行不同剂量梯度试验。试验设置了档剂量。在禾本科杂草生长二叶期、阔叶杂草生长 2 片真叶期时，将类似配方例 2 所制备的 3、16、17 号活性物乳油制剂用水稀释，以表 5 所示剂量对培养的试材进行茎叶喷雾处理，处理后 28 天，按照表 2 中确定的标准进行评定，结果见表 5。

表 5：苗后茎叶处理的除草活性剂量梯度试验

化合物编号	剂量 (g ai/ha)	除草效果					
		稗草	马唐	牛筋草	芥菜	反枝苋	马齿苋
3	375	5	5	5	4	5	4
	150	4	3	4	2	4	4
	75	2	0	3	4	4	4
16	375	5	5	4	5	5	4
	240	5	4	4	3	5	4
	124	4	4	4	3	5	2
17	375	5	5	5	4	5	5
	150	5	5	5	4	5	5
	75	5	4	4	2	5	4

试验实例 4：苗后茎叶处理的作物安全性试验

在装有试验土的 12cm 盆钵内分别播种棉花、油菜种子，置于 20—25℃温室中生长，待生长到一定时期后，将类似配方例 2 所制备的各号活性物乳油制剂用水稀释，以 375、150、75g ai/ha 的剂量对培养的试材进行茎叶喷雾处理。处理后定期观察植株生长状态和受害症状，处理后 28 天

表 6：出苗后叶面处理的作物安全性（旱田条件）

化合物编号	剂量(g ai/ha)	作物安全性	
		油菜	棉花
2	375	1	0
	150	0	0
	75	0	0
3	375	1	0
	150	0	0
	75	0	0
17	375	1	0
	150	0	0
	75	0	0